

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

## PCT

To:

OGILVY RENAULT  
1600 - 45 O'Connor Street  
Ottawa, Ontario K1P 1A4  
CANADA

RECEIVED

FEB 18 2005

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT AND  
THE WRITTEN OPINION OF THE INTERNATIONAL  
SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Date of mailing (day/month/year) 17/02/2005	
Applicant's or agent's file reference 15186-46PCT	<b>FOR FURTHER ACTION</b> See paragraphs 1 and 4 below
International application No. PCT/IB2004/003559	International filing date (day/month/year) 29/10/2004
Applicant ART ADVANCED RESEARCH TECHNOLOGIES INC. <b>ART. 19 AMEND. DUE: APRIL 17 2005</b>	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

**Filing of amendments and statement under Article 19:**  
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO, 34 chemin des Colombettes  
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**


Shortly after the expiration of 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within 19 months from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later); otherwise, the applicant must, within 20 months from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of 30 months (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the PCT Applicant's Guide, Volume II, National Chapters and the WIPO internet site.

Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Sandra Pozzi
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## NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>15186-46PCT</b>	<b>FOR FURTHER ACTION</b> <small>see Form PCT/ISA/220 as well as, where applicable, item 5 below.</small>	
International application No. <b>PCT/IB2004/003559</b>	International filing date (day/month/year) <b>29/10/2004</b>	(Earliest) Priority Date (day/month/year) <b>31/10/2003</b>
Applicant  <b>ART ADVANCED RESEARCH TECHNOLOGIES INC.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. 6

☒ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB2004/003559

A. CLASSIFICATION OF SUBJECT MATTER  
 C 7 G01N21/64 A61B5/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, INSPEC

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	<p>US 6 321 111 B1 (PERELMAN LEV T ET AL)            20 November 2001 (2001-11-20)            column 2, line 19 - line 28</p> <p>column 3, line 10 - line 24            column 4, line 42 - line 62            column 5, line 21 - line 24            column 6, line 49 - column 7, line 32            column 7, line 47 - line 49            column 9, line 17 - line 59            column 13, line 39 - line 47            equation 6            figures 1A, 6A, 6B, 7, 12</p> <p style="text-align: center;">-/-</p>	<p>1-12,            24-27            13-23,            28-42</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

\*&\* document member of the same patent family

Date of the actual completion of the international search

10 February 2005

Date of mailing of the international search report

17/02/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax (+31-70) 340-3016

Authorized officer

D'Alessandro, D

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/IB2004/003559

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4 135 816 A (NIEMANN ET AL) 23 January 1979 (1979-01-23) column 5 - column 6 column 8, line 56 - line 64 figures 1,3 -----	13-23, 28-42
X	HAIYONG QUAN ET AL INSTITUTE OF ELECTRICAL AND ELECTRONICS ENGINEERS: "A new 3d fluorescence imaging method" PROCEEDINGS OF THE IEEE 29TH. ANNUAL NORTHEAST BIOENGINEERING CONFERENCE. NEWARK, NJ, MARCH 22 - 23, 2003, PROCEEDINGS OF THE IEEE ANNUAL NORTHEAST BIOENGINEERING CONFERENCE, NEW YORK, NY : IEEE, US, vol. CONF. 29, 22 March 2003 (2003-03-22), pages 333-334, XP010647884 ISBN: 0-7803-7767-2 the whole document -----	1,24
A	WO 02/093143 A (XENOGEN CORPORATION) 21 November 2002 (2002-11-21) page 19, line 18 - page 21, line 15 page 4, line 24 - page 7, line 10 -----	1,9,10, 18,19,28
A	US 6 615 063 B1 (NTZIACHRISTOS VASILIS ET AL) 2 September 2003 (2003-09-02) column 2, line 34 - column 3, line 54 column 12, line 45 - column 18, line 25 column 22, line 25 - line 49 figures 2A,8A,8B -----	1-42

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB2004/003559

Patent document cited in search report		Publication date	Patent family member(s)	Publication -- date
US 6321111	B1	20-11-2001	US 5919140 A	06-07-1999
			US 6070583 A	06-06-2000
			WO 9626431 A1	29-08-1996
US 4135816	A	23-01-1979	DE 2603069 A1	11-08-1977
			SE 436661 B	14-01-1985
			SE 7700667 A	29-07-1977
WO 02093143	A	21-11-2002	CA 2447262 A1	21-11-2002
			EP 1402243 A2	31-03-2004
			JP 2004528916 T	24-09-2004
			WO 02093143 A2	21-11-2002
			US 2003002028 A1	02-01-2003
US 6615063	B1	02-09-2003	AU 2867302 A	03-06-2002
			CA 2428462 A1	30-05-2002
			EP 1349490 A2	08-10-2003
			JP 2004514150 T	13-05-2004
			WO 0241760 A2	30-05-2002
			US 2004015062 A1	22-01-2004

# PATENT COOPERATION TREATY

*Chapter II Demand  
already on docket NB.  
PCT*

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/IB2004/003559

International filing date (day/month/year)  
29.10.2004

Priority date (day/month/year)  
31.10.2003

International Patent Classification (IPC) or both national classification and IPC  
G01N21/64, A61B5/00

Applicant  
ART ADVANCED RESEARCH TECHNOLOGIES INC.

### 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

### 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office - P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk - Pays Bas  
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl  
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Authorized Officer

D'Alessandro, D

Telephone No. +31 70 340-1919





WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/IB2004/003559

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/B2004/003559

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 9,18

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 9,18 are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☒ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/IB2004/003559

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**Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-8,10-17,19-42
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-8,10-17,19-42
Industrial applicability (IA)	Yes: Claims	1-8,10-17,19-42
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

10/577527

APPROVED 28 APR 2006

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/IB2004/003559

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

With reference to the feature of claims 9, 18:

obtaining the scatter coefficient and the lifetime of the fluorophore using time-domain optical measurement of the medium;

there is no teaching in the application description (see page 11, l. 11-13), about how the skilled person could carry out the claimed method, starting from the embodiment disclosed in the application. These claims therefore lack support (Art. 6 PCT), and no opinion on novelty and inventive step was given.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

- D1: US-B1-6 321 111 (PERELMAN LEV T ET AL) 20 November 2001 (2001-11-20)  
D2: US-A-4 135 816 (NIEMANN ET AL) 23 January 1979 (1979-01-23)

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-8, 10-17, 19-42 does not involve an inventive step in the sense of Article 33(3) PCT.

1. The document D1 is regarded as being the closest prior art to the subject-matter of claim 1, and discloses (the references applying to this document):

*col. 2, l. 19-28*

A method determining depth of a volume comprising a fluorophore in a turbid medium using time domain (TD) optical fluorescence,

- |                             |   |
|-----------------------------|---|
| <i>col. 6, l. 49-52;</i>    | i) obtaining at least one temporal point spread function          |
| <i>col. 6, l. 61 -</i>      | (TPSF) by injecting light at an injection point at an             |
| <i>col. 7, l. 6;</i>        | excitation wavelength of said fluorophore and detecting           |
| <i>figs. 6A, 6B</i>         | light at a detection point at an emission wavelength of           |
|                             | said fluorophore;   |
| <br><i>col. 7, l. 8-23;</i> | ii) determining a time $t_{1/2}$ , at which the TPSF signal       |
| <i>fig. 7</i>               | reaches half-maximum;   |
|                             | iii) correlating said $t_{1/2}$ with said depth, to determine the |
|                             | depth, wherein said depth is insensitive to fluorophore           |
|                             | concentration.  |

The subject-matter of claim 1 differs from these disclosures of D1, in that the time instant correlated with the fluorophore depth is the time  $t_{\max}$  corresponding to the maximum of the fluorescence curve and not the rise-time  $t_{1/2}$  of D1.

However, the dependence of  $t_{\max}$  from the fluorophore depth, in certain conditions, is shown in document D1 (fig. 6A). Therefore, said time instant merely represents a known alternative to the use of  $t_{1/2}$  of D1, that the person skilled in the art would choose without an inventive effort depending on the circumstances. For these reason, the subject-matter of claim 1 does not involve an inventive step (Art. 33(3) PCT).

2. Dependent claims 2-27 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step. These claims actually refer to design options that are common in the art (see also documents D1, D2 and the passages cited in the search report).  
In the following paragraphs, brief additional reasons are given regarding the main features of these claims.

2.1 The generation of a tomographic image (claims 24, 25) is disclosed by document D1 (*col. 9, l. 17-24*).

2.2 The measurement of the fluorophore concentration by detecting the fluorophore emission intensity (claims 13-23) is well-known in the art (see for example document D2, *col. 8, l. 56-64*).

2.3 The correlation of fluorophore depth and fluorescence intensity (claim 26), for the measurement of the fluorophore concentration, is obvious for the person skilled in the art. It is actually well-known that the intensity depends on the concentration and on the depth of the fluorophore (see also document D1 *col.7, l. 47-49*).

2.4 The speed of light (depending on the refractive index) and the scattering coefficient of the medium, as in claims 5,10-12,17,19-21, are parameters that the person skilled in the art would take into account when performing these measurements (see D1, *col. 37-59; col. 13, l. 39-47; eq. 6; fig. 12*).

3. Document D1 discloses also the following features of the apparatus of independent claim 28:

<i>Fig. 1A;</i>	An apparatus [suitable] for determining the depth and
<i>col. 4, l. 42-56</i>	the concentration of a fluorophore in a turbid medium,
	comprising:
	a light source (10), optically coupled to a source
	channel (14) and said object (16), to inject light in said
	object at a desired point and excitation wavelength;
	a detector channel (18), optically coupled to a photon
	detector (22) and said object,
<i>col. 4, l. 56-62</i>	in a backreflection geometry relative to said source
	channel,
<i>col. 5, l. 21-24</i>	to acquire at least one temporal point spread function
	from a desired point to determine depth of said
	fluorophore;
<i>col. 5, l. 16-20;</i>	a depth calculator (24).
<i>col. 7, l. 8-13</i>	

The feature: "means for spatially positioning the object relative to the channel" is clearly included in the apparatus of D1.

The subject-matter of claim 28 also includes the features:

A) a second detector channel in a trans-illumination geometry relative to the source

channel, to measure an emission intensity of said fluorophore;  
B) a concentration calculator;

The technical problem addressed by these features is the measurement of the fluorophore concentration by detecting the intensity of the fluorescence radiation emitted by the object. Document D2 discloses an apparatus for measuring the concentration of a chemical in a sample (*col. 5, l. 5-11; col. 8, l. 56-62*), by means of fluorescence detection in a trans-illumination geometry (see in *figs. 1,3* the arrangement of lamp 5, mirror 12, sample vessel 11, emission filter 24 and detector 16). Features A and B are therefore disclosed by D2, solving the same technical problem as in the present application.

The person skilled in the art knows that, in the apparatuses like in D1, several detection channels may be added, according to the circumstances. Therefore, to solve the technical problem stated above, the skilled person would not need an inventive effort to implement in the apparatus of D1 a trans-illumination channel, as disclosed by D2, therefore reaching the subject-matter of claim 28. The subject-matter of claim 28 does not therefore involve an inventive step (Art. 33(3) PCT).

3.1 Dependent claims 29-42 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, because they represent common design options in the field.

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